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PI(s) of MSM U01: Chantal Darquenne, PhD
Institution(s): University of California, San Diego
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Abstract Authors

Andrew P. Kuprat[1], Richard A. Corley[2], Bahman Asgharian[3], Chantal Darquenne[4].
Pacific Northwest Natl Lab, Richland, WA[1], Greek Creek Toxicokinetics Consulting, LLC, Boise, ID[2], Applied Research Associates, Inc., Raleigh, NC[3], University of California, San Diego, CA[4].

Abstract Text

Chronic lung diseases, such as COPD and asthma, are among the leading causes of lost workdays, disabilities, and are the third most prevalent disease-based cause of death in the U.S. COPD is generally associated with exposure to toxic/irritant aerosols and adversely affects the quality of life for millions of susceptible individuals. Also, the lungs have been exploited as a potential route for local and systemic delivery of therapeutic aerosols for COPD, asthma, or other diseases where drugs may not be as effective by other routes of administration. As a result, the development of predictive aerosol dosimetry models has been a major focus of environmental toxicology and pharmaceutical health research for decades. Simplified compartmental and one-dimensional models have been successful in predicting overall deposition but fail to accurately predict local deposition. Computational fluid dynamics (CFD) has been extensively used to study flow patterns and aerosol transport in idealistic, physiologically realistic and more recently patient-specific models of lung airways. To date, the challenge of predicting the deposition of inhaled aerosols under disease conditions is largely unmet. However, these latter models provide the capability of including subject-specific lung abnormalities resulting from respiratory diseases. Yet, CFD studies typically only include a sub-region of the lung because of the prohibitive computational costs compared to simplified models. Thus, there is a need for developing multiscale strategies to link different models that apply to different regions of the lung so that a realistic subject-specific picture of the fate of inhaled aerosol in the lungs can be obtained. This is the main objective of this project. We are developing models through a step-wise, modular integration of 3D computational fluid dynamic (CFD) airflow and aerosol tracking CT-based models that extend from the nose and mouth to the conducting airways of the lung with each 3D pulmonary airway bi-directionally coupled with lower dimensional airflow, aerosol transport, and tissue mechanics models to describe aerosol transport and deposition over the full respiratory system. In the first few months of this project, we have focused on bi-directionally coupling our existing 3D/CFD aerosol transport models for healthy humans with individualized 1D Navier-Stokes airflow and particle transport and deposition models based upon the widely used Multiple Path Particle Deposition Model (MPPD) to form a foundation for simulations of aerosol inhalation, deposition, and exhalation over the entire respiratory system and full breathing cycle. These multiscale models will be evaluated and further refined using a rich database of multi-modal 3D imaging and aerosol deposition measurements in human volunteers that include both healthy and COPD cohorts. The expected outcome of our work is a suite of modular, multiscale models and standardized approaches for new model development that can be used by researchers, risk assessors, or clinicians to predict aerosol deposition in the lungs of humans under healthy and disease conditions in addition to the underlying algorithms and framework for effective linking of user-defined, personalized aerosol dosimetry models in the future.